

AMENDMENTS TO THE CLAIMS

This listing will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1(Canceled).

2(Currently Amended). The ~~method~~ model according to claim 1 17, wherein said model is a high penetrance model of said disorder and wherein said selected peptide is a naturally-occurring, recombinant or synthetic MHC class II-restricted T cell determinant that specifically binds with high affinity to said TCR.

3(Currently Amended). The ~~method~~ model according to claim 2, wherein at least 50% of said progeny before selection develop said autoimmune disorder.

4(Currently Amended). The ~~method~~ model according to claim 2, wherein said TCR is the TS1 TCR and said determinant is A/PR/8 hemagglutinin (HA) peptide S1.

5(Currently Amended). The ~~method~~ model according to claim 4, wherein said first mammal is a transgenic mouse that expresses MHC class II-restricted TCR with high affinity for an A/PR/8 hemagglutinin (HA) peptide S1 and said second mammal is a transgenic mouse that expresses DNA encoding the influenza A/PR/8 HA peptide S1 operably linked to a functional fragment of the MHC class II I-E α promoter.

6(Currently Amended). The ~~method~~ model according to claim 1 17, wherein said model is a low penetrance model of said disorder and wherein said selected peptide is a naturally-occurring, recombinant or synthetic protein or peptide fragment that binds with low affinity to said TCR.

7(Canceled).

8(Currently Amended). The ~~method~~ model according to claim 6, wherein said TCR is the TS1(SW) TCR and said peptide is A/PR/8 hemagglutinin (HA) peptide S1.

9(Currently Amended). The ~~method~~ model according to claim 8, wherein said first mammal is a transgenic mouse that expresses a MHC class II-restricted TCR with high affinity for an synthetic mutant S1 analog of A/PR/8 HA, but with low affinity for the native A/PR/8 HA S1 peptide; and wherein said second mammal is a transgenic mouse that expresses DNA encoding the native influenza A/PR/8 HA S1 peptide operably linked to a functional fragment of the MHC class II I-E α promoter.

10(Currently Amended). The ~~method~~ model according to claim 9, wherein said mutant analog is an HA peptide SEQ ID NO: 2 differing by two amino acids from said A/PR/8 HA S1 peptide SEQ ID NO: 1.

11(Currently Amended). The ~~method~~ model according to claim ~~1~~ 17, wherein in said second mammal a first nucleic acid sequence encoding said selected peptide is operably linked to a second nucleic acid sequence that directs expression of said first nucleic acid sequence selectively to MHC class II positive cells.

12(Currently Amended). The ~~method~~ model according to claim 11, wherein said second nucleic acid sequence ~~encodes~~ comprises a promoter sequence selected from the group consisting of the MHC class II I E α E- α gene promoter, non-MHC class II sequences involved in expression of the invariant chain, non-MHC class II H2-M promoter, the Dec205 promoter and the Cd11c promoter.

13(Canceled).

14(Currently Amended). The ~~method~~ model according to claim 17, wherein said autoimmune disorder is inflammatory arthritis.

15(Currently Amended). The ~~method~~ model according to claim 14, wherein said disorder is characterized by inflamed joints with bone resorption, mononuclear cell infiltrates and pannus formation.

16(Canceled).

17(Currently Amended). A non-human mammalian model of an autoimmune disorder, produced by the method ~~of claim 1~~ comprising
(a) producing intermated progeny of a first and a second transgenic non-human mammal of the same species, wherein said first mammal expresses a major histocompatibility (MHC) class II-restricted T cell receptor (TCR) and said second mammal expresses a selected peptide that binds to said TCR, which selected peptide is selectively expressed by MHC class II positive antigen presenting cells (APC) of said second mammal; and
(b) selecting from said progeny those mammals that co-express said TCR and said selected peptide,
wherein said selected progeny develop an autoimmune disorder.

18-19(Canceled).

20(Original). A transgenic non-human mammal that expresses a major histocompatibility (MHC) class II-restricted T cell receptor (TCR) and expresses a selected peptide that binds to said TCR, which selected peptide is selectively expressed by MHC class II positive antigen presenting cells (APC), wherein said mammal develops the phenotypic symptoms of an autoimmune disorder.

21-45(Canceled).

46(New): The transgenic mammal according to claim 20, wherein all germ cells and somatic cells of said mammal contain at least one transgene comprising a first nucleic acid sequence that encodes a major histocompatibility (MHC) class II-restricted T cell receptor (TCR) operably linked to regulatory sequences directing its expression; and a second nucleic acid sequence that encodes a selected peptide that binds to said TCR, operably linked to a sequence that directs expression of said selected peptide selectively to MHC class II positive antigen presenting cells (APC).

47(New): The transgenic mammal according to claim 20, wherein said selected peptide is a naturally-occurring, recombinant or synthetic MHC class II-restricted T cell determinant that specifically binds with high affinity to said TCR, and wherein said mammal exhibits high penetrance of said disorder.

48(New): The transgenic non-human mammal according to claim 47, wherein the phenotype is conferred by at least one transgene contained in somatic and germ cells of said mammal which directs said co-expression of said selected peptide selectively by its APC and said TCR.

49(New): The transgenic mammal according to claim 20, wherein said selected peptide is a naturally-occurring, recombinant or synthetic protein or peptide fragment that binds with low affinity to said TCR, and wherein said mammal exhibits low penetrance of said disorder.

50(New): The transgenic mammal according to claim 20, wherein said TCR is the TS1 TCR and said determinant is A/PR/8 hemagglutinin (HA) peptide S1.

51(New): The transgenic mammal according to claim 20, wherein all germ cells and somatic cells of said mammal express MHC class II-restricted TCR with high affinity for an A/PR/8 hemagglutinin (HA) peptide S1 and express DNA encoding the influenza A/PR/8 HA peptide S1 operably linked to a functional fragment of the MHC class II I-E α promoter.

52(New): The transgenic mammal according to claim 20, wherein said TCR is the TS1(SW) TCR and said peptide is A/PR/8 hemagglutinin (HA) peptide S1.

53(New): The transgenic mammal according to claim 20, wherein all germ cells and somatic cells of said mammal express a MHC class II-restricted TCR with high affinity for an synthetic mutant S1 analog of A/PR/8 HA, but with low affinity for the native A/PR/8 HA S1 peptide; and express DNA encoding the native influenza A/PR/8 HA S1 peptide operably linked to a functional fragment of the MHC class II I-E α promoter.

54(New): The transgenic mammal according to claim 53, wherein said mutant analog is an HA peptide SEQ ID NO: 2 differing by two amino acids from said A/PR/8 HA S1 peptide SEQ ID NO: 1.

55(New): The transgenic mammal according to claim 20, wherein all germ cells and somatic cells of said mammal comprise a first nucleic acid sequence encoding said selected peptide operably linked to a second nucleic acid sequence that directs expression of said first nucleic acid sequence selectively to MHC class II positive cells.